Reply to Gohar on 'Lungs, methotrexate and psoriasis', a comment on 'Fatal, incidental, idiopathic pulmonary fibrosis in a patient receiving long-term low-dose methotrexate for psoriasis'

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Lungs, methotrexate and psoriasis: reply from author

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Thank you for your interest in our case report and discussion.[1] Pulmonary fibrosis arising in association with methotrexate therapy was first reported in the 1970s in the context of cancer chemotherapy with very high doses given (up to 3.5g/m^2). Such patients accumulated a very high dose e.g. 41g over a few weeks.[2] In this specific

clinical scenario it is possible that methotrexate was causative although interestingly, the same author comments a year later that there are often many confounding factors e.g. use of concomitant agents which may also have pulmonary toxicity. They state, in practice, cytotoxic drug-induced lung disease may be difficult to establish with certainty because other potential causes of pulmonary disease are frequently present.[3] Experimental mouse models have shown that administration of very high daily doses of methotrexate (3mg/kg) for 5 weeks causes pulmonary fibrosis.[4] However, again, this is quite different from the low weekly doses of methotrexate given for psoriasis in clinical practice. Direct extrapolation from both these examples is not possible. Also, it should be emphasised that many apparent case reports of "pulmonary fibrosis" arising in the context of methotrexate treatment for psoriasis are in fact spurious including your reference 6 in which Karadag *et al* describe a case of resolving interstitial pneumonitis NOT fibrosis. With regards to the Japanese populations alluded to with psoriasis and interstitial pneumonia (IP) it is with interest that the prevalence of IPs is greater than the background prevalence of the most common form of chronic IP which is idiopathic pulmonary fibrosis (IPF).[5] Regarding our patient, we suggest that there were 2 possibilities –

1. There was no connection between his psoriasis and interstitial lung disease; the apparent correlation was a coincidence.
2. There was a correlation between his psoriasis and interstitial lung disease in that both disorders shared underlying immunological pathways.

The same argument applies to the role of methotrexate in interstitial lung disease (ILD); active role or innocent bystander? We do not believe that methotrexate had any negative effect on the natural history of the ILD. Correlation does not prove

causation. We agree that there may be a group of patients with psoriasis who are at increased risk of developing ILD and identifying these individuals is desirable. However, at the present time we do not believe that routine chest CT scanning is indicated nor any blind preventative medical treatments both of which may have side-effects. Further discussion and debate is desirable.

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